

Diethylhexyl Phthalate, Juvenile Exposure, Mice

CAS #117-81-7

Swiss CD-1 mice, at 0.0, 0.01, 0.025, 0.05% in feed

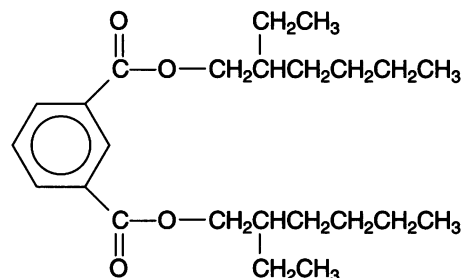
Carole A. Kimmel, NTP/NIEHS Project Officer

Catherine J. Price, Rochelle W. Tyl, Melissa C. Marr,

Christina B. Myers, and Brian M. Sadler, Research Triangle Institute

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Diethylhexyl phthalate (DEHP), a widely used plasticizer, was tested to determine the effects of prenatal administration on reproduction and fertility in Swiss CD-1 mice (Lamb et al., Toxicol Appl Pharmacol 88:255-269 [1987]). The test DID NOT follow the standard RACB protocol. Instead, the F_0 generation was exposed to DEHP in feed and levels that showed minimal maternal toxicity but had previously produced developmental toxicities. Exposure concentrations were set at 0.0, 0.01, 0.025, and 0.05% in feed. These concentrations produced calculated consumption estimates of 19, 48, and 95 mg/kg/day. Mice were given DEHP-containing feed from gestational days 0 to 17, whereupon only control feed was provided. The number and weights of F_1 pups were measured during lactation, and they were monitored for developmental landmarks (incisor

eruption, eye opening, wire grasping, testes descent, vaginal opening). Spontaneous locomotor activity was measured in doughnut-shaped track mazes at 4 times up to postnatal day 50. F_1 mice were maintained on control feed and until mating within dose groups at postnatal day 52 to 57. Females were allowed to deliver, and pups were nursed until postnatal day 4, when all F_2 pups were killed and discarded. Because a significant effect was noted for these F_2 litters, a crossover mating of F_1 mice was performed in an attempt to identify the affected sex. The pups were delivered and evaluated as above and killed on postnatal day 4.

There were no effects on F_0 dams' body weight, adjusted liver weight, feed, or water consumption. There was a 20% reduction in live pups per litter, and a tripling of prenatal mortality (as evidenced by uterine examination postmortem). Pup weight per

litter was unaffected, as was number of litters per treatment group. These dams showed no clinical signs of toxicity.

The F_1 pups showed no treatment effects on the acquisition of the developmental landmarks, nor on spontaneous locomotor activity.

In the F_1 mating trial, the fertility and mating indices were unaffected by previous gestational exposure to DEHP.

In a crossover test to determine the affected sex, no effects or changes were observed either in treated male or control female, or treated female or control male pairings.

The high dose F_1 females showed a 4% decrease in body weight at postnatal day 1. However, no other changes were observed. Neither F_0 nor F_1 males were evaluated.

In summary, no effects were observed for reproductive toxicity in either generation.

DIETHYLHEXYL PHTHALATE, JUVENILE EXPOSURE, MICE

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: PB84181734

Chemical: Diethylhexyl Phthalate

CAS#: 117-81-7

Mode of exposure: Feed

Species/strain: Swiss CD-1 mice

F ₀ generation	Dose concentration →	0.01%	0.025%	0.05%
General toxicity		Male, female	Male, female	Male, female
Body weight		•, —	•, —	•, —
Liver weight ^a		•, —	•, —	•, —
Mortality		•	•	•
Feed consumption		•, —	•, —	•, —
Water consumption		•, —	•, —	•, —
Clinical signs		•	•	•

Reproductive toxicity			
\bar{x} litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	—	—

F ₁ generation	Dose concentration →	0.01%	0.025%	0.05%
General toxicity		Male, female	Male, female	Male, female
Mortality		•	•	•
Adult body weight		•, —	•, —	•, ↓
Clinical signs		•	•	•

Reproductive toxicity			
Fertility index	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —

Summary information
F ₁ more sensitive than F ₀ ? No
Postnatal toxicity: No

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change (p<0.05); —, —, no change in males or females. ^aAdjusted for body weight.